BEST

Board on Environmental Studies and Toxicology

Overview of NRC Report:
RESEARCH PROGRESS ON ENVIRONMENTAL, HEALTH, AND SAFETY ASPECTS OF ENGINEERED NANOMATERIALS

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member,
Committee to Develop a Research Strategy for Environmental, Health, and Safety (EHS) Aspects of Engineered Nanomaterials (ENMs)

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

Committee

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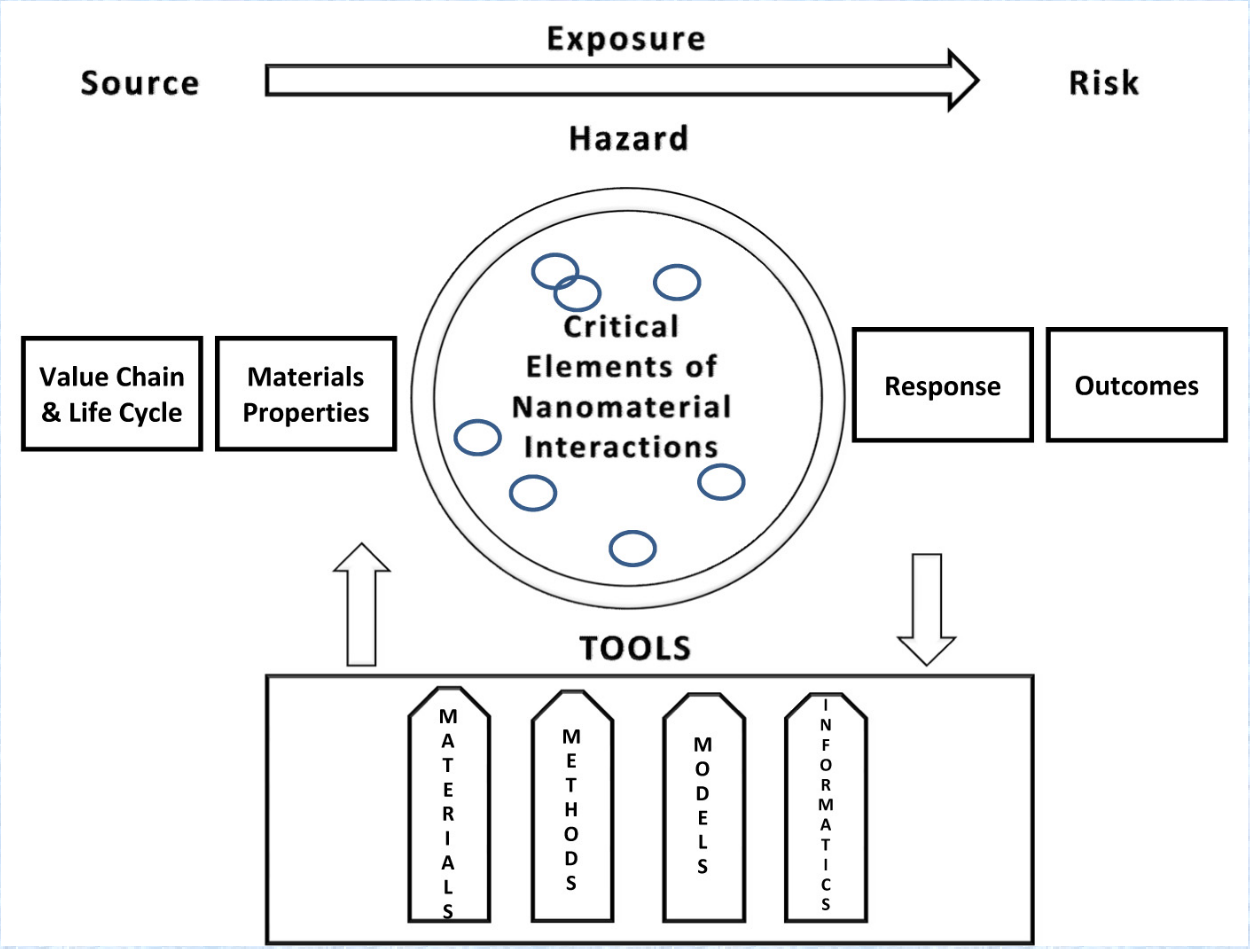
Statement of Task

- Develop and monitor implementation of an integrated research strategy to address EHS aspects of ENMs.
- <u>First report</u>:
  - Create conceptual framework for EHS-related research.
  - Develop research plan with short- and long-term research priorities.
  - Estimate resources to implement research.
- <u>Second report</u>:
  - Evaluate research progress.

First Report -Key Messages

- Strategic approach for developing science and research infrastructure – integrated, coordinated, evolving
- Conceptual framework structures approach
  - Value-chain and lifecycle perspective
  - Focus on properties of the materials and their influence on hazard/exposure
- Framework guides identification of critical research gaps
- Shapes research priorities
- Mechanisms for implementation as important as research priorities themselves

Conceptual Framework



Research Priorities

- Committee identified 4 broad, high-priority categories:
- ***Identification, characterization, and quantification of the origins of nanomaterial releases.***
- ***Processes that affect both potential hazards and exposure***
- ***Nanomaterial interactions in complex systems ranging from subcellular systems to ecosystems.***
- ***Adaptive research and knowledge infrastructure for accelerating research progress and providing rapid feedback to advance research.***

Second Report–Task Questions

- What research progress has been made in understanding health, environmental, and safety aspects of nanotechnology? How does research progress affect relevance of the initial set of research priorities?

- How have market and regulatory conditions changed and how does this affect research priorities?

- Are criteria for evaluating research progress on the health, environmental, and safety aspects of nanotechnology appropriate?

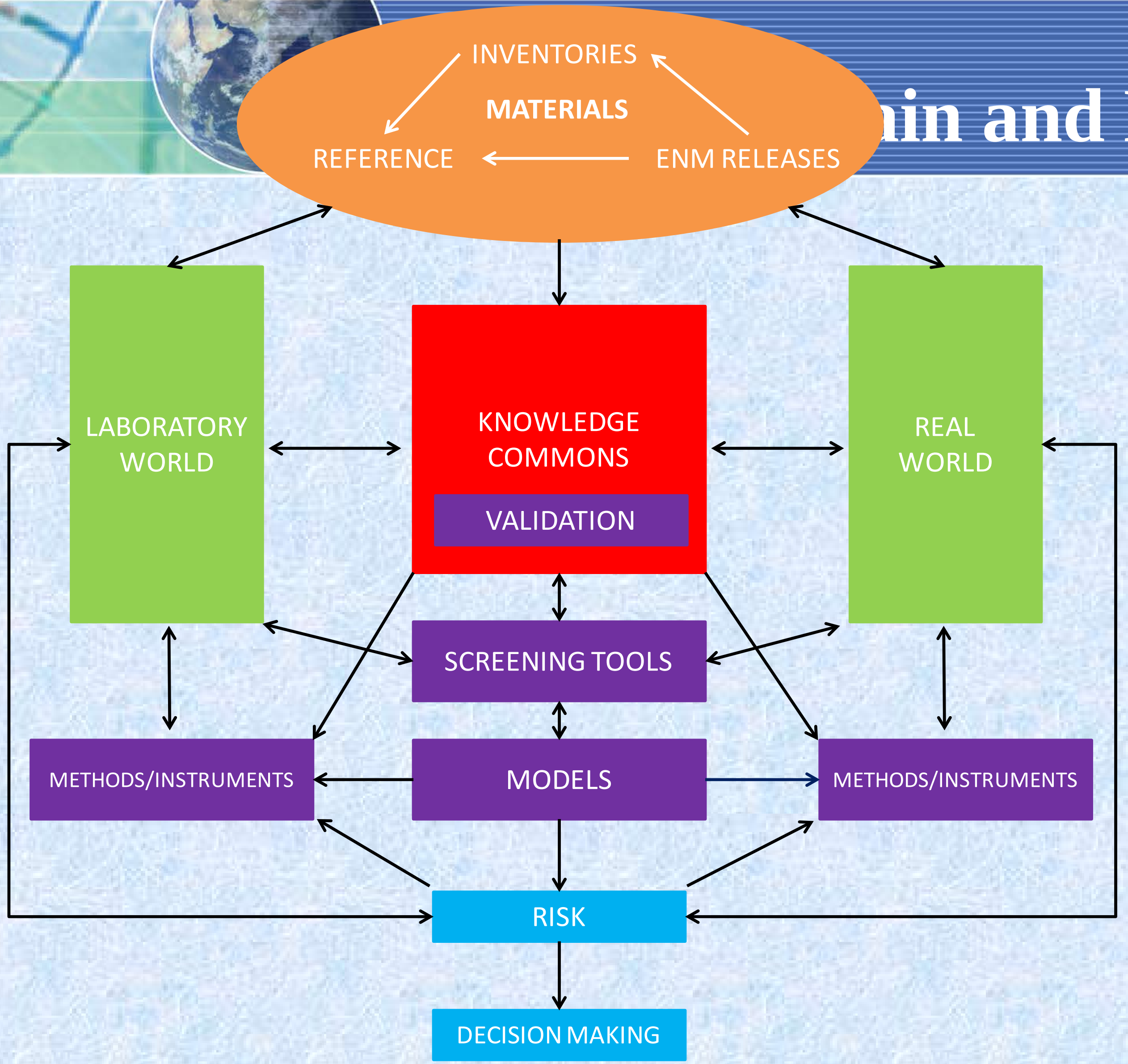
- Considering criteria developed, to what extent have short-term and long-term research priorities been initiated and implemented?

Committee Approach

- Indicators developed in first report, used to assess progress in this second report.
  - research
  - implementation

- Because of short timeframe since first report, trajectory of progress assessed, using qualitative rating scheme based on committee consensus.
  - **Green** substantial progress
  - **Yellow** moderate or mixed progress
  - **Red** little progress (minimal activity and little change expected)

in and Life Cycle



Nanotechnology environmental, health, and safety research enterprise

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Research Indicators

Adaptive Research and Knowledge Infrastructure for Accelerating Research Progress and Providing Rapid Feedback to Advance the Research

- Extent of development of libraries of well-characterized nanomaterials, including those prevalent in commerce and reference and standard materials
- Development of methods for detecting, characterizing, tracking, and monitoring nanomaterials and their transformations in simple, well-characterized media
- Development of methods to quantify effects of nanomaterials in experimental systems.
- Extent of joining of existing databases, including development of common informatics ontologies
- Advancement of systems for sharing the results of research and fostering development of predictive models of nanomaterial behaviors

Research Indicators

Quantifying and Characterizing the Origins of Nanomaterial Releases

- Developing inventories of current and near-term production of nanomaterials
- Developing inventories of intended uses of nanomaterials and value-chain transfers
- Identifying critical release points along the value chain
- Identifying critical populations or systems exposed
- Characterizing released materials in complex environments
- Modeling nanomaterial releases along the value chain

Research Indicators

Processes That Affect Both Exposure and Hazard

- Steps taken toward development of a knowledge infrastructure able to describe the diversity and dynamics of nanomaterials and their transformations in complex biologic and environmental media
- Progress in developing instrumentation to measure key nanomaterial properties and changes in them in complex biologic and environmental media
- Initiation of interdisciplinary research that can relate native nanomaterial structures to transformations that occur in organisms and as a result of biologic processes
- Extent of use of experimental research results in initial models for predicting nanomaterial behavior in complex biologic and environmental settings

Research Indicators

Nanomaterial Interactions in Complex Systems Ranging from Subcellular Systems to Ecosystems

- Extent of initiation of studies that address the impacts of nanomaterials on a variety of endpoints in complex systems, such as studies that link in vitro to in vivo observations, that examine effects on important biologic pathways, and that investigate ecosystem effects
- Extent of adaptation of existing system-level tools (such as individual species tests, microcosms, and organ-system models) to support studies of nanomaterials in such systems
- Development of a set of screening tools that reflect important characteristics or toxicity pathways of the complex systems described above
- Steps toward development of models for exposure and potential ecologic effects
- Identification of benchmark (positive and negative) and reference materials, for use in such studies and measurement tools and methods to estimate exposure and dose in complex systems

Research Progress – Getting to Green

Nanomaterial sources and development of reference tools

- Nanotechnology EHS research community has relied on commonly available ENMs to conduct most studies.
  - No process for determining which nanomaterials should have high priority for development based on research needs
- Elements for advancing development and distribution of reference materials for research and analytic purposes to get to green include:
  - Mechanism for identifying and setting priorities among nanomaterials for development
  - Adoption and use of appropriate and standardized material descriptors for design, development, and sharing of ENMs
  - Improved synthesis and purification methods for ENMs
  - Collaboration among scientists to optimize materials for study
  - New methods and approaches for rapid characterization of reference materials
  - Instrumentation for characterizing complex nanoscale species
  - Information-management plans and appropriate research infrastructure for collecting information on nanomaterial production and uses.

Research Progress – Getting to Green

Fundamental processes that affect nanomaterial exposure and hazard

- Research occurs in both the laboratory world and real world.
  - Involves experimental approaches to understand the physical, chemical, and biologic processes that affect exposure and hazard.
- Continued efforts to elucidate mechanisms of ENM interactions with organisms and ecosystems are critical for achieving long-term goal of predicting ENM effects
  - Requires advances in instrument development and
  - Improved data-integration infrastructure

Research Progress – Getting to Green

Informatics: The Knowledge Commons

- Focal point of research enterprise
- Locus for collaborative development of methods, models, and materials
  - Requires increased integration with research in laboratory world and real world, and with materials development
- Strength lies in ability to knit existing and new capabilities in an overarching framework that allows linkage of components of nanotechnology EHS research
  - Such integration has not yet occurred
- Play key role in integrating participation of all sectors−government and academic researchers, NGOs, regulators, and industry−to generate data and knowledge required as inputs.

Research Progress – Getting to Green

Model Development

- Development of suite of models for predicting physical characteristics of ENMS, outcomes of toxicity testing, and exposures is an important outcome of knowledge commons.

- Some progress in development of some types of models
  - lack of consistency in approaches and interoperability of data to support effective model development.

- Getting to green will require substantial data development from mechanistic and complex-system studies and characterization of physical properties of a variety of ENMs in different environments.
  - Initial models will need to be developed iteratively using emerging data.

Research Progress – Getting to Green

Methods and Instrumentation

- Tools required for detecting and characterizing ENMs and their properties in relevant media.

- Progress in development of methods and instrumentation has varied because of different applications of the tools
  - Some progress in characterizing newly manufactured ENMs in well-understood, simple media
  - Little progress in detecting and characterizing ENMs in complex environments.

- Additional progress will require characterization and quantification of properties of ENMs in complex biologic and environmental media and measurement of properties of single particles
  - so that specific ENM properties can be associated with observed behaviors and effects.

Research Progress – Getting to Green

Nanomaterial Interactions in Complex Systems Ranging from Subcellular to Ecosystems

- Research cuts across both the laboratory world and real world.
- Lack of mechanistic data is critical barrier to advancing understanding of ENM interactions in complex systems
  - ➢ An increasing volume of toxicity data is being generated, but ability to use data to predict ENM risks with any certainty is constrained due to types of studies conducted.
- Studies need to focus on more complex experimental-design issues−relevant doses; dose-response relationships and time-course characteristics; appropriate target cells, tissues, and organisms; and examination of more biologic pathways
  - ➢ Together with better characterization of ENM test substances and use of standardized reference materials as controls
- Data should be shared among investigators, and results of in vivo studies should be compared with results of in vitro screening assays
- Validated screening tools also need to be developed.

Mechanisms to Ensure Research Implementation

- Interagency Coordination
- Stakeholder Engagement in the Research Strategy
- Public-private partnerships
- Management of Potential Conflicts of Interest

Concluding remarks

- Characterization of risks posed by ENMs is:
  - a scientific challenge requiring integrated, quantitative, and systems-level approaches.
  - an institutional challenge that stretches the conventional roles of agencies and researchers.
    - Empowered leadership at federal level with oversight by single agency would begin to address many organizational barriers.
    - Sustained funding for research and for infrastructure to support data sharing is needed.
- Ideal of responsible nanotechnology development is both daunting and important, but it is attainable.